REMARKS

Claims 1-8 and 10-13 are pending in the application. New Claim 14 has been added. Claim 9 is withdrawn from consideration as being drawn to a non-elected invention. Applicants expressly reserve the right to file divisional applications or take such other appropriate measures deemed necessary to protect the inventions in the remaining claim. Claims 1, 2, 3, 8, 10 and 11 (and thus their respective dependent claims) have been amended. Support for the new claim and amendments can be found in the specification as filed. No new matter has been added by way of amendment. Reexamination and reconsideration of the claims are respectfully requested.

Hyperlinks

The Examiner has objected to the disclosure due to the inclusion of hyperlinks on page 26, line 15 and page 27, line 26. Applicants have amended the specification to remove the hyperlinks, thereby obviating this objection.

Title

The Examiner has objected to the title of the invention as not being descriptive of the instant invention. Applicants have amended the title to "MAIZE PR1-C10 PATHOGENESIS-RELATED POLYNUCLEOTIDE, TRANSFORMED PLANTS, AND METHODS OF USE IN MODULATING PR1-C10 EXPRESSION", in order to more clearly indicate the invention to which the claims are directed. This amendment is shown in the previous section entitled "Amendments to the Specification", beginning on page 2 of the instant response. No new matter is added by way of the amendment to the title.

Abstract

The Examiner has objected to the abstract of the invention as not being descriptive of the instant invention. Applicants have amended the abstract as shown in the previous section entitled "Amendments to the Specification", beginning on page 2 of the instant response. Applicants assert that the new abstract is clearly indicative of the invention to which the claims are directed. No new matter is added by way of the amendment to the abstract.

Claim Objections

The Examiner has objected to claims 1-3 and 10-11 because of informalities. The Examiner has further provided suggested amendments to overcome these informalities. Applicants have amended claims 1-3 and 10-11 according to the Examiner's suggestions, thereby obviating the claim objections.

The Rejection of Claims Under 35 U.S.C. §112, First Paragraph, Should be Withdrawn

Enablement

The Examiner has rejected claims 1-8 and 10-13 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully disagree.

The Examiner states that the instant specification fails to provide guidance for exact hybridization or amplification conditions and probes/primers to use in isolation of nucleic acids other than SEQ ID NOs: 1 and 3. Applicants respectfully disagree. Applicants have provided extensive guidance to be used in the selection of stringency conditions based on the desired outcome. See page 22, line 8 through page 24, line 3 of the specification as originally filed. Applicants have provided an extensive discussion of hybridization conditions and requirements specifically on page 22, line 18 to page 23, line 3 of the instant specification. Applicants have also provided guidance for post-hybridization wash conditions on page 23, line 4 through page 24, line 3, of the specification. The design of appropriate primers has been outlined by the Applicants on page 34, lines 5-29 of the specification. Furthermore, Applicants have given guidance regarding the design and use of probes on page 37, lines 4-26 of the specification. In view of the extensive guidance provided, Applicants assert that the invention is clearly enabled as claimed. However, in order to further prosecution, Applicants have amended claims 1 and 10 to remove reference to nucleic acids that hybridize to sequences of the present invention under stringent conditions.

The Examiner further states that Applicants have failed to provide adequate guidance for making nucleic acids with 85% identity to SEQ ID NO: 1 or 3, nucleic acids comprising 20

contiguous nucleotides of SEQ ID NO: 1 or 3, vectors and expression cassettes comprising those nucleic acids, cells, plants and seeds comprising the vector, and a method of using the expression cassette to modulate the level of PR1-C10 in a plant.

In support of this rejection, the Examiner cites Lazar *et al.* who teach that a conservative substitution reduced biological function while "nonconservative" substitutions had no effect. Likewise, the Examiner cites Hill *et al.* who teach that ADP-glucose pyrophosphorylase proteins mutated to substitute arginine for histidine (a "conservative" substitution), reduced the enzymes activity. The Examiner concludes that "without specific guidance as to which amino acids to modify, substitutions cannot be reliably made in proteins."

Amended claims 1 and 10 recite: "... an isolated nucleic acid molecule, *wherein said nucleic acid molecule encodes a polypeptide with PR1-C10 activity,* selected from the group consisting of ...." (emphasis added). Thus, in the amended claims, only those variants *having PR1-C10 activity* are claimed.

The specification clearly states on page 61, lines 19-23: "Guidance as to appropriate amino acid substitutions that *do not affect desired biological activity* of the native protein may be found in the model of Dayhoff *et al.* (1978) *Atlas of Protein Sequence and Structure* (Nat'l Biomed. Res. Found., Washington, D.C.), herein incorporated by reference. Conservative substitutions, such as exchanging one amino acid with another having similar properties, may be preferable.." (emphasis added). The disclosure plainly acknowledges that conservative substitutions per se, *may* not produce a *functional* protein, but is one of many tools the skilled artisan may use to produce a nucleic acid of the currently claimed invention.

Applicants wish to point out that both references use the known homology to related proteins to identify and target particular amino acid residues. These references use homology to predict important conserved amino acids where substitution with another amino acid would actually be likely to have an impact on the activity of the protein. For example, Lazar *et al.* shows that even conservative substitution of L48 with similar amino acids (M or I) dramatically impacted activity, as predicted by the observed absolute conservation of leucine (L) at this position. In all cases, the modified protein had to be screened for the effect(s) of the modification. Clearly, one of skill in the art does believe that structural identity, as well as the

presence of functional domains and conserved motifs are predictive of polypeptide function, as is clearly demonstrated by the pervasive use of sequence searching algorithms such as BLAST, FASTA, and the like, and multiple sequence alignment programs such as CLUSTAL and PileUp, and the like. Accordingly, one of skill in the art could use the known homology to related proteins to identify and target particular amino acid residues where substitution with another amino acid would actually be *unlikely* to have an impact on the activity of the protein.

The screening of a group of sequences containing from a few to many, inoperative species in order to isolate one or more operative species is a common practice in many aspects of the biotechnological arts. With the guidance provided in the specification as cited herein, isolation of operative embodiments from a group of candidate sequences as claimed in amended claims 1 or 10, clearly has a reasonable expectation of success by one skilled in the art.

The Examiner states that it is not clear that the instant nucleic acid actually encodes a protein that participates in the pathogenic response and enhances disease resistance. The Examiner states that the specification states that SEQ ID NO: 1 has only 50-60% identity to maize PR-1 genes, but provides no evidence that SEQ ID NO: 1 actually encodes a protein with PR-1 actvity. Applicants attach an alignment of known PR-1 genes from a variety of species including *Arabidopsis* (GenBank Accession No. NP-201460), maize (GenBank Accession No. T02054), and tobacco (GenBank Accession No. S10205) compared to the protein sequence of the instant invention (SEQ ID NO: 2, indicated as SID_2 on the alignment). The alignment indicates identical amino acids in yellow and highly conserved amino acids in green (using the model of Dayhoff *et al.* discussed supra). This alignment clearly shows the high similarity between the PR-1 gene of the present invention and other PR-1 genes known in the art and is evidence of the membership of SEQ ID NO: 2 in the PR-1 gene family. As stated on page 2, lines 21-28 of the specification as originally filed, pathogenesis-related proteins are known to be associated with the defense response and can be used to develop transgenic plants with enhanced disease resistance.

The Examiner has also rejected claims 1-8 and 10-13 because the specification does not disclose a repeatable process to obtain the nucleic acids (of Patent Deposit No. PTA-1688) and it is not apparent if the nucleic acids are really available to the public. Applicants direct the attention of the Examiner to page 14, line 27 to page 15, line 4 of the specification as originally filed, which

clearly states that the deposit of the nucleic acids was made at the Patent Depository of the American Type Culture Collection, Manassas, Virginia, on April 11, 2000, and assigned Patent Deposit No. PTA-1688. Furthermore, the specification clearly states that this deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. The undersigned agent for Applicants hereby states that the deposits will be irrevocably and without restriction released to the public upon the issuance of a patent.

Written Description

The Examiner has rejected claims 1-8 and 10-13 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner states that the Applicants have not, in fact, described DNA molecules that have 85% identity to SEQ ID NOs: 1 or 3, that comprise 20 contiguous nucleotides of SEQ ID NOs: 1 or 3, or that hybridize to SEQ ID NOs: 1 or 3. In view of the claim amendments previously discussed, DNA molecules that have 85% identity to SEQ ID NOs: 1 or 3, that comprise 20 contiguous nucleotides of SEQ ID NOs: 1 or 3, or that hybridize to SEQ ID NOs: 1 or 3 are no longer being claimed. Applicants assert that in view of the amendments to the claims and the arguments presented in the previous discussion of enablement, that the specification provides an adequate written description of the invention as it is now claimed.

Accordingly, Applicants request that the rejections of claims 1-8 and 10-13 under 35 U.S.C. §112, first paragraph, be withdrawn.

The Rejection of Claims Under 35 U.S.C. §112, Second Paragraph, Should be Withdrawn

The Examiner has rejected claims 1-8 and 10-13 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

Applicants have amended claims 1 and 10 to recite the sequence deposited as Patent Deposit No. PTA-1688, in order to clarify the claims. Applicants have also amended claims 1 and 10 to refer to PR1 activity, rather than PR1-C10-like activity. The C10 part of the name of the gene is Applicants' own name for the gene and is not representative of any special activity of the gene of the instant invention.

Applicants have amended claims 1 and 10 to remove parts of the claims which recite high stringency conditions.

Applicants have amended claim 8 in accordance with the Examiner's suggestion to state that the seed comprises the vector.

Applicants have amended claim 10 to correct the antecedent basis and have also amended claim 10 to overcome the rejections involving inducing expression and omitted steps.

Accordingly, Applicants respectfully request withdrawal of the rejections of claims 1-17 under 35 U.S.C. §112, second paragraph.

The Rejection of Claims Under 35 U.S.C. §102 Should be Withdrawn

The Examiner has rejected claims 1-2 and 4 under 35 U.S.C. §102(b) as being anticipated by Ryals *et al.* (WO 95/19443). Ryals *et al.* teach an isolated tobacco nucleic acid that comprises a region of 31 nucleotides with 90.3% identity to SEQ ID NO: 1 and 3 that would hybridize under "high stringency conditions" to SEQ ID NO: 1. Ryals *et al.* do not teach the maize PR-1 gene of the present invention. In view of the amendments to claims 1 and 10, in which only those sequences having at least 95% identity to SEQ ID NO: 1 or 3 are claimed, Applicants respectfully point out that the sequence taught by Ryals *et al.* does not anticipate the amended claims.

The Examiner has also rejected claims 1-8 and 10-13 under 35 U.S.C. §102(b) as being anticipated by Bloksberg *et al.* (1998, US Patent No. 5,850,020). Bloksberg *et al.* teach an isolated nucleic acid that comprises 42 contiguous bases of SEQ ID NO: 1. Bloksberg *et al.* do not teach the maize PR-1 gene of the present invention. In view of the amendments to claims 1 and 10 which removed reference to nucleic acids comprising at least 20 contiguous nucleotide

bases of SEQ ID NOs: 1 and 3, Applicants assert that the amended claims are not anticipated by the sequence of Bloksberg *et al.*

Accordingly, Applicants request the withdrawal of the rejections of claims 1-8 and 10-13 U.S.C. §102(b).

CONCLUSION

In view of the above amendments and remarks, Applicants submit that the rejections of the claims under 35 U.S.C. §§112, first and second paragraphs and 35 U.S.C. §102 have been overcome. Applicants respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject Application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR §1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-1852.

Respectfully submitted,

Claire L. Moxon

Claire L. Moxon
Agent for Applicant(s)
(See: LIMITED RECOGNITION
UNDER 37 CFR § 10.9(b)
SUBMITTED 6-17-2003)

PIONEER HI-BRED INTERNATIONAL, INC.
Corporate Intellectual Property
7100 N.W. 62nd Avenue
P.O. Box 1000
Johnston, Iowa 50131-1000
Phone: (515) 253-2162
Facsimile: (515) 334-6883

Multiple Sequence Alignment Results

```
Symbol comparison table: blosum62.cmp CompCheck: 1102

                 GapWeight: 8
           GapLengthWeight: 2

 NP_201460_pileup_141691.txt  MSF: 224  Type: P  June 23, 2003 17:50
Check: 8653 ..

 Name: S10205 (tobacco)       Len:   224  Check: 9782  Weight:  1.00
 Name: T02054 (maize)         Len:   224  Check: 4346  Weight:  1.00
 Name: NP_201460 (Arabidopsis)Len:   224  Check: 8631  Weight:  1.00
 Name: SID_2  (maize)         Len:   224  Check: 5894  Weight:  1.00

//
            1                                                    50
     S10205 ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~MGFVL FSQMPSFFLV
     T02054 ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~MAPRLACL
  NP_201460 ~~~~~~~~~~ ~~~~~~MALA HHAAFVALLA ISVKAISPAA A.LKPK..QI
      SID_2 MAHSRSHHHL LLLPAPMATA CLLLATLLAL CAAPAPTHGA RVLMPG..GA

            51                                                   100
     S10205 SAALLFLIIS LSCGAQNSPQ AYLDAHNTAR ADVGVEPLTW DDQVAAYAQN
     T02054 LAAAMAAIVV APCTAQNSPQ AYVDPHNAAR ADVGVGPVSW DDTVAAYAQS
  NP_201460 VSTSPPPPPT ISAAAKAFAD ....AHNKAR AMVGVPPLVW SQTLEAAARR
      SID_2 GAVTKAQQGG TGSGSNATAD EYLAPHNQAR AAVGVAPLRW NAGLASAAAG

            101                                                  150
     S10205 YAS.Q.LAAD CMLVHSH.GQ YGENLAWGS. GDFMTAAKAV EAWVNEKQYY
     T02054 YAA.QR.QGD CKLIHSG.GP YGENLFWGSA GADWSASQAV GSWVSEKQYY
  NP_201460 LARYQRNQKK CEFASANPGK YGANQLWAKG LVAVTPSLAV ETWVKEKPRY
      SID_2 TVAQQRRQGG CAFADVGASP YGANQGWASY .RA.RPAEVV ALWVAEGRYY

            151                                                  200
     S10205 DHDSNTCAQG .QVCGHYTQVV WRNSVRVGCA RAQC.NSGGY VVSCNYDPPG
     T02054 DHDTNSCAEG .QVCGHYTQVV WRDSTATGCA RVVCDNNAGV FISCSYNPPG
  NP_201460 NYKSDTCAAN HT.CGVYKQVV WRNSKEAGCA QASCAKESTV LTACFYNPPG
      SID_2 THANNTCAAG RQ.CGTYTQVV WRNTAEVGCA QASCATGAT. LTLCLYNPHG

            201                      224
     S10205 NFVGQSPYEL KRRPFHVIYV RTSA
     T02054 NVVGESPY~~ ~~~~~~~~~~ ~~~~
  NP_201460 NVIGQKPY~~ ~~~~~~~~~~ ~~~~
      SID_2 NVQGQSPY~~ ~~~~~~~~~~ ~~~~
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